Analytical Seminar

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"Digital Resolution Detection of miRNA by Photonic Resonator Outcoupler Microscopy"

Circulating exosomal miRNA represents a potentially useful class of bloodborn biomarkers for cancer, which, for specific sequences, can be correlated with clinical outcomes. Existing approaches such as qRT-PCR are capable of providing low limits of detection and dynamic range that spans five orders of magnitude though enzymatic amplification, rigorous calibration, and careful reaction timing. We seek to develop an alternative approach that is highly specific for a target miRNA sequence with a simple, rapid workflow, and the ability to provide "digital" resolution of individual target molecules with high signal-to-noise ratio, in an inexpensive instrument. We present the initial proof-of-concept of such an assay, in which gold nanoparticle tags are prepared with thermodynamically optimized nucleic acid toehold probes that, when binding to a target miRNA sequence, displace a probe-protecting oligonucleotide and reveal a capture sequence that is used to selectively pull down the target-probe-nanoparticle complex to a photonic crystal (PC) biosensor surface. By matching the surface plasmon resonant wavelength of the nanoparticle tag to the resonant wavelength of the PC nanostructure, the reflected light intensity from the PC is dramatically and locally quenched by the presence of each individual nanoparticle, enabling a new form of biosensor microscopy that we call Photonic Resonator Absorption Microscopy (PRAM). Dynamic PRAM imaging of nanoparticle tag capture, which requires two highly specific nucleic acid binding interactions to signal the presence of each miRNA target, enables 100 aM limits of detection in a 30-60 minute assay, using only a single step. The talk will describe the optical operating principles of PROM, the thermodynamic design of DNA toehold probes, and our first results demonstrating the detection limits, selectivity, and dynamic range of the assay. The talk will also describe our vision for utilizing the technology for daily monitoring of multiple miRNA targets in the context of gauging the effectiveness of advanced prostate cancer treatment.

Thursday
October 4

12:15 p.m.
1315 Chemistry

Refreshments at 12 p.m.

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